

Ted Sanders Presented at RNC Meeting July 26th, 2004

Population Data (Review)

- Black males have a higher rate of malignant diseases of the respiratory system (lung cancer), despite reportedly smoking fewer cigarettes/day

<u>Year</u>	<u>Age-Adjusted Death Rates</u>			
	<u>Males</u>		<u>Females</u>	
	<u>Black</u>	<u>White</u>	<u>Black</u>	<u>White</u>
1995	80.5	53.7	27.8	27.9

Epidemiology

- If the fact that Black male smokers have a higher age-adjusted rate of lung cancer than white male smokers can be attributed to menthol cigarettes, one should be able to see such a difference in an epidemiological study

Epidemiology

- Four relatively large studies have been conducted:
 - American Health Foundation Multi-Center Case-Control Study (Kabat and Hebert, *Cancer Res.*, 1991)
 - Kaiser Permanente Prospective Study (Sidney, et al., *Arch. Intern. Med.*, 1995)
 - Los Angeles County Case-Control Study (Carpenter, et al., *Ann. Epidemiol.*, 1999)
 - Multi-Center Case-Control Study (Brooks, et al., *Am. J. Epidemiol.*, 2003)

American Health Foundation

Risk of Lung Cancer by Mentholated Cigarette Use Among Current Smokers

<u>Gender</u>	<u>No. of Cases</u>	<u>Years of use of mentholated cigarettes</u>			
		<u>Never</u> <u>RR</u>	<u>1-14</u> <u>RR^b</u>	<u>15+</u> <u>RR^b</u>	<u>Ever^a</u> <u>RR^b</u>
Male	588	1.00	1.14	0.98	1.06
Female	456	1.00	0.82	0.76	0.78
Comb.	1044	1.00	1.02	0.88	0.94

a. At least one year mentholated use

b. Adjusted for age, race, education, cigarettes/day, inhalation, duration of smoking, BMI

American Health Foundation

- Conclusion of the authors:

"Use of mentholated cigarettes was not associated with increased risk of lung cancer or of specific histological types of lung cancer in this study."

"If our results are confirmed by other researchers, the implication would be that use of mentholated cigarettes does not explain Black-White differences in lung cancer incidence or time trends."

Kaiser Permanente Study

Risk of Lung Cancer by Mentholated Cigarette Use Among Current Smokers

<u>Gender</u>	<u>No. of Cases^b</u>	<u>Years of use of mentholated cigarettes</u>			
		<u>Never</u> <u>RR</u>	<u>1-9</u> <u>RR^a</u>	<u>10-19</u> <u>RR^a</u>	<u>20+</u> <u>RR^a</u>
Male	158 (57)	1.00	1.10	1.32	1.59
Female	132 (42)	1.00	0.72	1.01	0.70
Comb.	290 (99)	1.00	0.93	1.17	1.10

a. Adjusted for age, race, education, years of smoking and cigarettes/day

b. First number is total number of cases; number in parentheses is number of mentholated cigarette smokers

Kaiser Permanente Study

- Conclusion of the authors:

"This study suggests there is an increased risk of lung cancer associated with mentholated use in male smokers but not in female smokers."

Los Angeles County Study

Risk of Lung Cancer by Pack-Years of Mentholated Cigarette Use Among Ever Smokers

<u>Race^a</u>	<u>No. of Cases</u>	<u>Pack-years of mentholated smoking</u>			
		<u>0</u>	<u>1-15</u>	<u>16-31</u>	<u>32+</u>
		<u>RR</u>	<u>RR^b</u>	<u>RR^b</u>	<u>RR^b</u>
White	181	1.00	1.01	1.01	1.06
Black	156	1.00	0.96	0.69	0.90
Both	337	1.00	1.05	0.92	0.95
Both (M)	202	1.00	0.87	1.21	1.48

a. White defined as Caucasian; Black defined as Afro-American; (M) denotes males

b. Adjusted for age, race, total pack years and years since quitting

Los Angeles County Study

- Conclusion of the authors:

"Our results suggest that the lung cancer risk from smoking mentholated cigarettes resembles the risk from smoking non-mentholated cigarettes. Our data do not support the hypothesis that the increased risk of lung cancer among African Americans is due to the increased prevalence of menthol smoking."

Multi-Center Case-Control Study

Risk of Lung Cancer by Mentholated Cigarette Use Among Current Smokers

		<u>Years of use of mentholated cigarettes</u>		
<u>Gender/ Race</u>	<u>No. of Cases</u>	<u>Never RR</u>	<u>1-15 RR^a</u>	<u>15+ RR^a</u>
Male	61	1.00	0.67	0.91
Female	53	1.00	1.14	1.00
White	76	1.00	0.86	1.01
Black	38	1.00	0.60	1.21

a. Adjusted for sex, age, race, year of interview, number of years smoking, cigarettes/day

Multi-Center Case-Control Study

- Conclusions of the authors:

“In summary, our results do not support the hypothesis that smoking menthol cigarettes increases the risk of lung cancer more than does smoking nonmenthol cigarettes. However, owing to the methodological limitations in our study and previous studies, the possibility of a modest increase in risk associated with menthol cigarettes cannot be excluded.”

Meta Analysis

Use of Mentholated Cigarettes

Relative Risk (95% CI)^{a,b}

<u>Male</u>	<u>Female</u>	<u>Combined</u>
1.05 (0.82-1.34)	0.85 (0.70-1.03)	0.97 (0.86-1.10)

Long-Term Use of Mentholated Cigarettes

1.13 (0.86-1.47)	0.78 (0.60-1.01)	0.95 (0.80-1.13)
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a. Only adjusted RRs or ORs used

b. Random effects meta-analysis; the only difference between fixed effects and random effects was for long-term use in males, which was 1.11 instead of 1.13.

Other Endpoints Investigated

- Esophageal Cancer (American Health Foundation Study) – No association for males; statistically non-significant increase for females. Authors conclude that there is no indication for the association of smoking of mentholated cigarettes with esophageal cancer.
- Other forms of cancer (Kaiser Permanente Study) – No increased association for any form of smoking-related cancer (lung cancer excluded, six other types of cancer investigated).

Other Endpoints Investigated

- North Carolina Prospective Study in Pregnant Women (Savitz, et al., *Epidemiology*, 2001) – A small case-control study that investigated the comparative association of non-mentholated and mentholated cigarettes with birth of small for gestational age (SGA) births from mothers smoking during pregnancy. Where comparisons were possible, smokers of mentholated cigarettes had a lower risk of SGA births than smokers of non-mentholated cigarettes, although differences were not statistically significant.

Epidemiology - Conclusions

- Epidemiological data do not support any increased risk for lung cancer in smokers of mentholated cigarettes compared to smokers of non-mentholated smokers
- Given, however, the fact that only four studies have been carried out coupled with the imprecision of epidemiological studies, the epidemiology does not rule out a modest increase in risk, although it would be difficult to account for the 50% increase in risk as indicated in the first slide of this part of the presentation.

Population Data (Revisited)

<u>Year</u>	<u>Age-Adjusted Death Rates</u>			
	<u>Males</u>		<u>Females</u>	
	<u>Black</u>	<u>White</u>	<u>Black</u>	<u>White</u>
1995 ^a	80.5	53.7	27.8	27.9
1995 ^b	115.1	82.6	38.8	41.1

a. U.S. Surgeon General, 1998; age-adjusted to the 1940 U.S. standard population

b. CDC, Health, United States, 2003; age-adjusted to the 2000 U.S. standard population

Black, White Ratio by Age

<u>Age</u>	<u>45-54</u>	<u>55-64</u>	<u>65-74</u>	<u>75-84</u>	<u>85+</u>	<u>All^a</u>
<u>Males</u>						
White	35.7	150.8	374.9	529.9	522.4	75.7
Black	70.7	223.5	488.8	642.5	562.8	101.1
Ratio	1.98	1.48	1.30	1.21	1.08	1.34
<u>Females</u>						
White	24.8	96.1	213.2	272.7	215.9	42.3
Black	32.9	95.3	194.1	224.3	185.9	39.8
Ratio	1.33	0.99	0.91	0.82	0.86	0.94

a. CDC, Health, United States, 2003; age-adjusted to the 2000 U.S. standard population

Epidemiology – Final Conclusions

- US black males have a higher age-adjusted rate of lung cancer than do US white males (34%)
- US black females have approximately the same age-adjusted rate of lung cancer as US white females
- Epidemiological data do not support the hypothesis that smokers of menthol cigarettes are at greater risk for lung cancer than smokers of non-menthol cigarettes
- The largest difference between black and white males occurs for the age range 45-54, and the second largest difference for the age range 55-64. This may possibly suggest a genetic effect, but lung cancer in the "young" is not well understood.